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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/020,419	12/13/2001	Audrey Goddard	P2637-1	5267

9157 7590 03/09/2004

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EXAMINER	
ANDRES, JANET L	
ART UNIT	**PAPER NUMBER**
1646	

DATE MAILED: 03/09/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/020,419	GODDARD ET AL.	
	Examiner	**Art Unit**	
	Janet L. Andres	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 December 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *19,21-23,27,31 and 32* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *19, 21-23, 27, 31, and 32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)

2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.

4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .

5) ☐ Notice of Informal Patent Application (PTO-152)

6) ☐ Other: _____.

RESPONSE TO AMENDMENT

1. Applicant's amendment filed 1 December 2003 is acknowledged. Claims 19, 21-23, 27, 31, and 32 are pending and under examination in this office action. The text of those sections of Title 35, U.S. Code, not included in this action can be found in a prior office action.

Claim Rejections/Objections Withdrawn

2. The objection to the specification pertaining to its reference to the priority data is withdrawn in response to Applicant's amendment clarifying the priority claims.

3. The objection to the title is withdrawn in response to Applicant's amendment removing the word "novel".

Claim Rejections Maintained/New Grounds of Rejection

4. The rejection of claims 19, 21-23, and 27 under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement is maintained for reasons of record in the office action of 9 July 2003 and applied to new claims 31 and 32.

The amended claims are now drawn to methods of using PRO4425 polypeptides or antibodies reacting with them to treat cartilage disorder. Claims 19, 21-23, 31, and 32 now encompass treatment of all forms of cartilage disorder, either by adding PRO4425 polypeptides or antibodies to them, which could be either agonistic or antagonistic; claim 27 is limited to the methods using the polypeptide to treat osteoarthritis.

Applicant argues that the expression of PRO4425 suggests that it is involved in regulating cartilage growth and maintenance. Applicants provide microarray data indicating that PRO4425 is overexpressed in osteoarthritis, indicating that PRO4425 is involved in cartilage development and is overexpressed in a disease state.

Applicant's arguments have been fully considered but have not been found to be persuasive. Neither the specification nor the prior art provide sufficient guidance as to how the artisan could use either PRO4425 proteins or antibodies to them to affect any cartilage disorder. As stated in the previous office action (p. 3, para.6), involvement in development does not provide guidance as to how the polypeptides, or effectors thereof, could be used to affect disease, because development is a complex process involving many factors with many roles. The fact that a polypeptide is expressed during chondrogenesis does not indicate what effect, if any, it has on chondrogenesis. The mere presence of a polypeptide provides no guidance as to its function, nor does the suggestion that it is "involved in" cartilage growth indicate how it might be involved and thus how it or an antibody to it could be used. Further, an effect during development does not indicate that it will have any effect on mature cartilage. See for example, Goldring, Current Rheumatology Reports, 2000, vol. 2(6), pp. 465-469, provided by Applicant in the information disclosure statement of May 2002. On p. 463, column 2, Goldring teaches that "resident articular chondrocytes are not capable of recapitulating the original development program". Thus, were an effect of PRO4425 during development to be established, it would not be predictive of an ability to affect disease, because mature cartilage differs from developing tissue in its responses. Similarly, overexpression during osteoarthritis is not predictive of any particular function. Factors that are both causal and protective are produced during osteoarthritis; it cannot be assumed that the presence of a factor indicates that it has a positive effect. See, for example, van den Berg, Zeitschrift for Rheumatologie, 1999, vol. 58(3), pp. 136-141, provided by Applicant in the information disclosure statement of May 2002, which teaches that chondrocytes produce both matrix proteoglycans and degrading enzymes during

osteoarthritis (p. 137, column 1, p. 140, figure 4). Thus, expression during chondrogenesis does not indicate what effect the polypeptide has on chondrogenesis, nor does expression in osteoarthritis indicate what effect the polypeptide has on arthritis. No particular activity is suggested for PRO4425 and thus for related polypeptides or for antibodies against them. As stated on p. 4 of the previous office action, all that is known about the activity of PRO4425 is that it affects glucose uptake and mesangial cell differentiation, neither of which is predictive of an effect on cartilage disorders. Thus, since the teachings with regard to expression fail to provide guidance as to how PRO4425 polypeptides or antibodies against them could be used, and the art provides no compensatory teachings as to the PRO4425's function, it would require undue experimentation for one of skill in the art to use the polypeptide or an antibody against it to affect any cartilage disorder.

5. The rejection of claims 19, 21-23, and 27 under 35 U.S.C.112, first paragraph, as lacking written description is maintained for reasons of record in the office action of 9 July 2003 and applied to new claims 31 and 32.

Applicant's amendment is insufficient to overcome this rejection. The basis of the rejection was that the genus of "PRO4425" molecules had not been identified, because no common structural features or other characteristics had been identified. Thus one of skill would be unable to identify other members of the genus. The amendments to claims 19, 21-23, and 27 do not provide any common characteristics for this polypeptide. No limitations to structure are provided by the claims, and the functional limitations require only that it, or an antibody against it, somehow affect a cartilage disorder. Thus the claims require no common structure or function, and the skilled artisan would not conclude that Applicant was in possession of the

broad genus of polypeptides encompassed by the designation "PRO4425". New claims 31 and 32 require a degree of similarity to the disclosed sequence, but, since the only functional limitation is that the polypeptide somehow affect a cartilage disorder, no common function is required. Since no structural features characteristic of PRO4425 are set forth in the specification, and no common function is required, for the reasons set forth above and in the office action of 9 July 2003, the artisan would not be able to identify the polypeptides encompassed by the claims. Thus the invention is not described so as to convey to one skilled in the art that Applicant was in possession of the polypeptides and of methods using them.

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claim 32 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

This claim is indefinite in the recitation of "stringent hybridization". Stringent hybridization conditions are not defined in the specification; what is provided on p. 15, lines 21-30, are examples. Thus one of skill in the art would not know what conditions, and thus what polypeptides, Applicant intended the claims to encompass.

NO CLAIM IS ALLOWED.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Janet L. Andres whose telephone number is 571-272-0867. The examiner can normally be reached on Monday-Thursday and every other Friday, 8:00-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached on 571-272-0871. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Janet L. Andres, Ph.D.
2 March 2004

JANET ANDRES
PATENT EXAMINER